Fifth International Symposium on Virtual Colonoscopy, October 2004

"Computer-Aided Detection for CT Colonography"

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I. Introduction

Beginning in approximately 1997, we began an investigation of automated detection for CT bronchography ("virtual bronchoscopy")(1-3). In our study published in 1998, we found that 100% of airway lesions 5 mm in size or larger could be detected by a shape-based detection algorithm(4). The specificity was 80%. This technology transferred readily to CT colonography (CTC), and, in association with colleagues at Stanford University, we published a feasibility study showing that colonic polyps could be detected in a phantom model(5). In 2001, we published the first study of computer-aided polyp detection for CT colonography to appear in a peer-reviewed journal, in association with colleagues at Mayo Clinic(6). These early results showed the feasibility of CT colonography computer-aided detection. In addition, they suggested that computer-aided detection might become an important part of the radiologist's assessment of CT colonography studies. In this syllabus, I present a brief overview of the current status of CT colonography computer-aided detection.

II. Rationale for Computer-Aided Detection

It has been shown that perceptual error reduces the sensitivity of CT colonography by 14% for polyps 1 cm in size or larger(7). Given the multitude of images in a CTC study, the causes of perceptual error are not mysterious. Depending upon the reconstruction interval, there can be 1,200 images or more to interpret. For example, images in the prone and supine position must be interpreted. Some investigators examine the colon antegrade and retrograde and in lung and soft tissue windows. Three-dimensional virtual endoscopic views may also be needed for problem solving. Interpretation times ranging from 10 – 60 minutes per study have been reported in the literature. Many reported studies used consensus readings of two radiologists, further lengthening interpretation time.

III. Principles of CAD

The purpose of computer-aided detection (CAD) is to locate possible polyps automatically and annotate the images or present a list of image locations. The radiologist reviews the output of the CAD and makes the final diagnosis.

The main function of the CAD software is to identify sites with features characteristic of polyps(8). Once these features are identified, the CAD software classifies sites of detection as polyps or false positive diagnoses. A suitable CAD system has high sensitivity for detection of clinically significant polyps (those over a size threshold, e.g. 0.5 or 1.0 cm) and a low number of false positive detections. All current CTC CAD systems produce on average at least one false positive detection per CTC examination.

Two useful features for CAD are surface shape and CT attenuation. Surface shape is an intuitive feature to identify polyps, as by definition a polyp is a surface distortion. Colonic polyps protrude inward from the wall of the colon into the lumen of the colon and are characteristically rounded in contour. In contrast, haustral folds tend to be circumferential and ridge-shaped.

CT attenuation has also been shown to be useful for CAD, particularly for distinguishing polyps from false positive diagnoses. False positive diagnoses tend to have low CT attenuation and polyps soft tissue attenuation. Residual stool may mimic a polyp but stool can sometimes be distinguished by the presence of gas bubbles within it.

A mathematical algorithm for computing shape is necessary to enable the computer to recognize such shapes. While there are a number of different methods for quantifying shape mathematically, we have found curvature to be an excellent shape descriptor(4). The principle behind curvature assessment is that each point on the surface of the colon can be described as having one of six elemental shapes: elliptical pit, elliptical peak, hyperbolic, cylindrical valley, cylindrical ridge and plane. Elliptical peak shapes are like the top of an ice cream cone. Elliptical pit shapes are like the inside of a hollow ball. Hyperbolic shapes are like a saddle. Cylindrical valley and ridge shapes are like the inside and outside of a pipe, respectively. Plane shapes are flat.

Polyps tend to have elliptical peak curvature (5). Haustral folds tend to have cylindrical or hyperbolic curvature. Normal colon between haustral folds tends to have plane, cylindrical, or elliptical pit curvature. We have found that approximately 91% of the colonic surface can be safely excluded from further analysis using this shape classification system(5). The remaining 9% of the colonic surface contains polyps and other structures, some of which the radiologist needs to review. Further processing can reduce the area in question to only 0.4% of the colonic surface. In a study of ten simulated 1 cm polyps inserted into a CT colonography study of an adult patient we found that all 10 polyps could be detected using the shape based algorithm. When further processing was applied to reduce false positives, 8 of the polyps could be located without any false positive diagnoses.

Once potential polyps are detected by CAD, they must be shown to the radiologist who makes the final diagnosis. There are a number of ways to do this. We have found it

useful to label sites directly on CTC images to show the radiologist where the tentative polyp detections may be found(9). These labels can be turned on or off so that they do not obscure the original images. To save time, the radiologist can jump directly to the labeled images. To evaluate the potential time efficiency of CAD, we applied CAD to a CTC study consisting of 161 images. The CAD software placed 7 CAD detections on 22 of the 161 images (some of the CAD detections spanned more than one image). The total interpretation time with these annotated images was only two minutes to locate a colonoscopically proven 1.5 cm polyp in the rectosigmoid colon. This result suggests that CAD may be able to sharply reduce interpretation times.

The two major approaches of doing CAD include identification of features and development of classification strategies. CAD for CT colonography benefits from years of radiology research in other areas of CAD, particularly mammography and lung nodule CAD. These areas of research have a rich history of two-dimensional and three-dimensional image analysis, statistical methods and classification strategies, some of which are readily transferable to CT colonography CAD.

IV. Current Status of CTC CAD

CT colonography computer-aided detection is in a preliminary stage of development(10). It is in early clinical trials at several academic centers. In this section, I summarize the published results of these trials. Particular attention is paid to whether statistical analyses (such as cross-validation) are performed that correct the overestimate of CAD performance on data from which it has been developed and optimized.

Our first clinical trial, performed in collaboration with colleagues at Mayo Clinic, was a study of 20 high risk subjects with known polyps(6). There were 28 polyps 1 cm or larger. Twenty – six of these could be found in retrospect on CTC. The sensitivity of the CAD algorithm was 64%, using a classification scheme that minimized the false positive detections to on average 6 false positive detections per colon. The sensitivity could be improved at the expense of an increase in false positive detections. Note that these results were obtained using supine CTC only. The sensitivity would be higher if prone CTC was added although the number of false positive detections would also be higher. When only polyps in well distended colonic segments were considered, the sensitivity increased to 71%. In this study, CT attenuation was used to reduce the number of false positive detections by 39% (to 3.5 false positive detections per colon). Processing took about 2 minutes on a common desktop computer.

Our second clinical trial applied the same CAD algorithm to a new database of patients from a surveillance population(11). These polyps proved to be difficult to identify, both by CAD and by radiologists. However, the CAD system found four polyps greater than 1 cm that were not detected by either of two radiologists and seven polyps greater than 1 cm that were not detected by both radiologists who independently interpreted the cases. There were an average of 11 false positive detections per patient for CAD.

Recent research at NIH Radiology has led to the development of novel methods of polyp segmentation and detection, including the use of deformable contours and similarity measures, and false positive reduction (12-16). We have also done work on improving the classifiers that distinguish true and false positive detections, including the application of "genetic" algorithms and "committees" of support vector machines(17-22). These improvements reduced the false positive rate by 36% and increased sensitivity by 7% in one application(20). To assess the error rates, we used an improved estimation technique known as smoothed leave-one-out cross-validation (22). Our group has recently presented preliminary data on the use of CAD in the setting of intravenous and oral contrast-enhanced CTC(23, 24).

The University of Chicago group assessed curvature in a thin layer that included the colonic wall(25-27). They analyzed "directional gradient concentration" and applied linear and quadratic discriminant analysis. They used a "leave-one-out" analysis to validate their results. In a study of 14 patients having 15 polyps less than or equal to 1 cm and 6 polyps greater than 1 cm, they found 100% sensitivity per patient. Their average false positive rate was 2.0 per patient. At a false positive rate of 2.0 per patient, their sensitivity for polyps was 90% (19 of 21). While conspicuity of polyps was not formally addressed, review of the cases and the published images reveals many were highly conspicuous and easy to find without CAD. This group has recently published work on CAD to detect colorectal masses and on a preliminary observer performance trial (28, 29).

Stanford University researchers have used a shape analysis of the colonic wall based upon the Canny edge detector and Hough transform operator(30, 31). In a study of 14 polyps greater than 8.5 mm in 9 patients, they found a sensitivity of 92.9% and 7.9 false positives per colon. In a refinement of their algorithm, they developed a random orthogonal shape selection (ROSS) technique based on statistical pattern recognition (32). In this method, randomly selected volumes in coronal, sagittal, and axial orientations are taken through potential polyps and then analyzed using statistical pattern recognition. The ROSS method included additional shape signatures which identified elliptical and linear shapes. The researchers utilized ten-fold cross validation and found that the ROSS method reduced false positives by 62%. However, this technique was time consuming, requiring hours of processing per subject. This group has also published results of an optical flow technique to reduce false positive detections(33, 34) and a surface normal overlap method(35).

Wake Forest University researchers published a shape and wall thickness analysis for CTC CAD in a conference proceeding article(36). They found 11 of 15 polyps measuring 0.5 to 4.0 cm in 10 patients (sensitivity 73%). There were on average 49 false positives per patient.

Researchers from Leuven used a shape analysis based on convexity and sphericality(37, 38). They found all 10 polyps 1 cm or larger in 18 patients. There were 8 false positives per CT colonography scan. In more recent work, they report a detection rate of 85% for polyps larger than 6 mm with a mean false positive rate per data set of 2.48 (39).

Researchers at Siemens have published preliminary results in several conference proceedings articles. They report 95% sensitivity on 19 polyps 6-20 mm in size with 8 FP per patient on a test set of data distinct from the training set (40). Their proprietary algorithm used moments of tissue intensity, volumetric and surface shape and texture characteristics. In another paper, they reported 95% sensitivity on 42 polyps 6-19 mm in size in 71 patients with 5.76 FP per patient (41).

V. Challenges Ahead

CT colonography computer-aided detection research is in an early stage but already is producing exciting results. There are many challenges ahead and one anticipates new and useful results in the near future(42).

Major research challenges are determination of useful features and improvement in classification strategies. The central objective of this research is to identify combinations of features that describe polyps so they cluster together and away from false positives in feature-space.

False positive reduction is an important goal for CAD researchers. Common causes of false positives are the ileocecal valve, stool, the enema tube tip, bulbous haustral folds, motion artifact and impressions on the colon by extracolonic structures (other bowel loops, the uterus or the liver)(11, 43). Ongoing research is addressing these issues (15). One example of such research is electronic bowel cleansing (stool subtraction) techniques.

It is important to properly match polyps seen on conventional colonoscopy and on CT colonography. Typically, conventional colonoscopy identifies polyps to within a colonic segment and even then considerable errors in location can occur. If a polyp on colonoscopy is matched to an incorrect location on the CTC examination, the efficacy of CAD can be impaired because the CAD system is trained on incorrect data.

A successful element of CAD may be to use the supine and prone CTC images together to find polyps and reduce false positives. For example, if a polyp is found in the same location on both supine and prone CTC, the confidence is high that this represents a true polyp. CAD may need to recognize such concordances.

There is a limited amount of available data to train and test CAD. While initial results often report high sensitivity and few false positives, when presented with new data CAD will typically have lower sensitivity with more false positives. This fact highlights the need for suitable training databases that researchers can use to validate the robustness of their CAD algorithms. The American College of Radiology Imaging Network (ACRIN) is undertaking a project to create such a database.

Cancer detection, while feasible with CAD, may be a less important use for CAD. It has been shown in a number of studies that CTC without CAD already has 100% sensitivity for detecting colon cancers (44).

The major clinical challenge will be to evaluate the impact of CAD in an actual clinical interpretive setting. Studies will need to show that CAD improves clinical sensitivity without placing an undue burden through reduced specificity or increased interpretation time. An early result suggests that CAD may decrease interobserver variability(45).

VI. Conclusions

Preliminary results in CT colonography CAD are encouraging. There is evidence that high sensitivity and a low number of false positive detections per examination are possible in the foreseeable future. However, these early results need to be confirmed on larger image databases. The application of CAD to clinical practice is also sure to provide interesting results that will propel further research.

VII. Acknowledgments

Andrew Dwyer, M.D., is thanked for critical review of the manuscript.

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